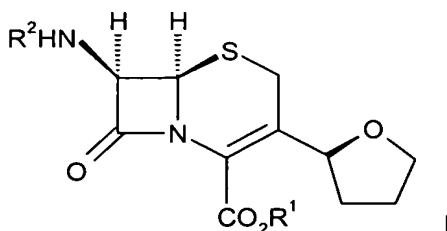
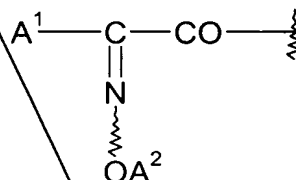


CLAIMS

1. A process for preparing a 3-cyclic-ether-substituted cephalosporin of the formula I:



5 or a pharmaceutically acceptable salt thereof,
wherein
the group CO₂R¹ is a carboxylic acid or a carboxylate salt; and
R² has the formula:

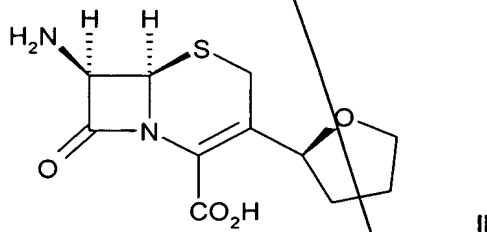


10 wherein

A¹ is selected from the group consisting of C₆₋₁₀aryl, C₁₋₁₀heteroaryl and C₁₋₁₀heterocyclyl;

A² is selected from the group consisting of hydrogen, C₁₋₆alkyl, C₃₋₁₀cycloalkyl, C₆₋₁₀aryl, C₁₋₆alkyl(CO)(C₁₋₆)alkyl-O-, HO(CO)(C₁₋₆)alkyl, mono-(C₆₋₁₀aryl)(C₁₋₆alkyl),
15 di-(C₆₋₁₀aryl)(C₁₋₆alkyl), and tri-(C₆₋₁₀aryl)(C₁₋₆alkyl);

comprising reacting a compound of formula II:



with a compound of the formula III:



20 wherein

R² is as defined above; and

L is selected from the group consisting of hydroxy, halo, azido, mono(C₁₋₆alkyl)carbonate, (C₁₋₆alkyl)carboxylate, (C₆₋₁₀aryl)carboxylate,

Sub
A4

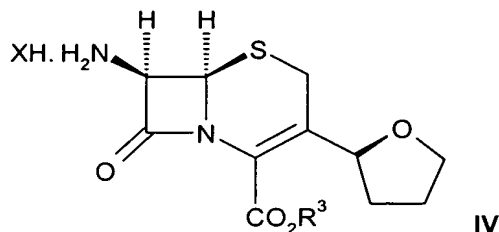
10006276-120404

Sub
A4

mono-(C₆₋₁₀aryl)(C₁₋₆alkyl)carboxylate, di-(C₆₋₁₀aryl)(C₁₋₆alkyl)carboxylate,
di-(C₁₋₆alkyl)phosphorothioate, (C₁₋₆alkyl)sulfonyl, mono-(C₁₋₆alkyl)(C₆₋₁₀aryl)sulfonyl,
di-(C₁₋₆alkyl)(C₆₋₁₀aryl)sulfonyl, (C₁₋₆alkyl)-(CO)-S-, cyano-C₁₋₆alkoxy, C₆₋₁₀aryloxy,
3-benzthiazolyloxy, 8-quinolinylloxy and N-oxy-succinimidyl;

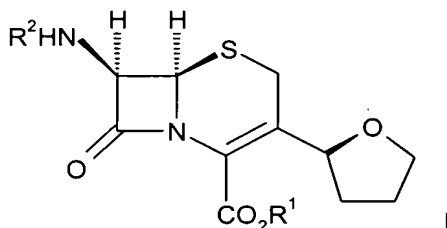
- 5 in the presence of a solvent, a base, an optional coupling agent and an optional catalyst.

2. The process according to claim 1 further comprising the step of preparing said compound of formula II by reacting a compound of formula IV:

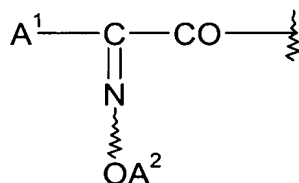


- 10 wherein R³ is para-nitrobenzyl or allyl; and X is halo;
with a suitable deprotecting agent; in the presence of a solvent.

3. A process for preparing a 3-cyclic-ether-substituted cephalosporin of the formula I:



- 15 or a pharmaceutically acceptable salt thereof,
wherein the group CO₂R¹ is a carboxylic acid or a carboxylate salt; and
R² has the formula:

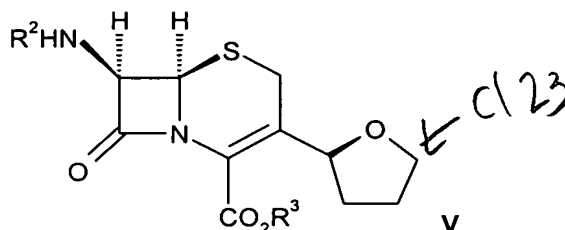


- 20 wherein A¹ is selected from the group consisting of C₆₋₁₀aryl, C₁₋₁₀heteroaryl and C₁₋₁₀heterocyclyl;

A² is selected from the group consisting of hydrogen, C₁₋₆alkyl, C₃₋₁₀cycloalkyl, C₆₋₁₀aryl, C₁₋₆alkyl(CO)(C₁₋₆alkyl)-O-, HO(CO)(C₁₋₆alkyl), mono-(C₆₋₁₀aryl)(C₁₋₆alkyl), di-(C₆₋₁₀aryl)(C₁₋₆alkyl) and tri-(C₆₋₁₀aryl)(C₁₋₆alkyl);

10006679 120401

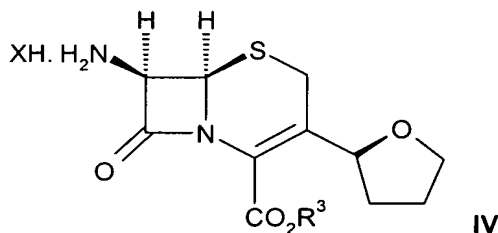
comprising reacting a compound of formula V:



wherein R² is as defined above; and R³ is para-nitrobenzyl or allyl;

with a suitable deprotecting agent in the presence of a solvent.

5 4. The process according to claim 3 further comprising preparing said compound of formula V by reacting a compound of formula IV:

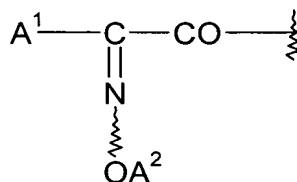


wherein R³ is para-nitrobenzyl or allyl; and X is halo;

with a compound of the formula III:

10 R^2L III;

wherein R² has the formula:



wherein A^1 is selected from the group consisting of C_{6-10} aryl, C_{1-10} heteroaryl and C_{1-10} heterocyclyl;

15 A² is selected from the group consisting of hydrogen, C₁₋₆alkyl, C₃₋₁₀cycloalkyl, C₆₋₁₀aryl, C₁₋₆alkyl(CO)(C₁₋₆)alkyl-O-, HO(CO)(C₁₋₆)alkyl, mono-(C₆₋₁₀aryl)(C₁₋₆alkyl), di-(C₆₋₁₀aryl)(C₁₋₆alkyl) and tri-(C₆₋₁₀aryl)(C₁₋₆alkyl); and

L is selected from the group consisting of hydroxy, halo, azido, mono(C₁₋₆alkyl)carbonate, (C₁₋₆alkyl)carboxylate, (C₆₋₁₀aryl)carboxylate, mono-(C₆₋₁₀aryl)(C₁₋₆alkyl)carboxylate, di-(C₆₋₁₀aryl)(C₁₋₆alkyl)carboxylate, di(C₁₋₆alkyl)phosphorothioate, (C₁₋₆alkyl)sulfonyl, mono-(C₁₋₆alkyl)(C₆₋₁₀aryl)sulfonyl, di-(C₁₋₆alkyl)(C₆₋₁₀aryl)sulfonyl, (C₁₋₆alkyl)-(CO)-S-, cyano-C₁₋₆alkoxy, C₆₋₁₀aryloxy, 3-benzthiazolyloxy, 8-quinolinylloxy and N-oxy-succinimidyl;

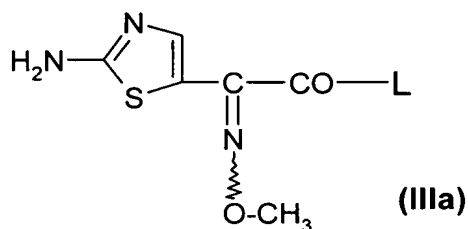
in the presence of a solvent.

5. The process according to claim 1, wherein said A¹ moiety of said R² is C₁₋₁₀heteroaryl selected from the group consisting of furyl, thienyl, pyridyl, aminothiazolyl and aminothiadiazolyl, wherein said amino moiety of said aminothiazolyl or aminothiadiazolyl is optionally protected.

6. A process according to claim 1, wherein said A² moiety of said R² is C₁₋₆alkyl.

7. A process according to claim 1, wherein L of said compound of the formula III is selected from the group consisting of halo, methanesulfonyl, diethylphosphorothioate and 3-benzthiazolyloxy.

8. A process according to claim 1, wherein said compound of formula III has a formula IIIa:



and wherein L is selected from the group consisting of halo, methanesulfonyl, diethylphosphorothioate and 3-benzthiazolyloxy.

9. A process according to claim 1, wherein said solvent is water, acetone, tetrahydrofuran, ethyl acetate, dimethylacetamide, dimethylformamide, acetonitrile, methylene chloride, 1,2-dichloroethane or mixtures thereof.

10. A process according to claim 1, wherein said solvent is water, acetone, or mixtures thereof.

11. A process according to claim 1, wherein a catalyst is used.

12. A process according to claim 11 wherein said catalyst is a Lewis acid catalyst selected from the group consisting of boron trihalide and aluminum halide.

13. A process according to claim 1 wherein said base is diisopropylethylamine or sodium hydroxide.

14. A process according to claim 1, wherein said coupling agent is selected from the group consisting of N,N'-diethylcarbodiimide, N,N'-dipropyl carbodiimide, N,N'-diisopropylcarbodiimide, N,N'-dicyclohexylcarbodiimide, N-ethyl-N'-[3-(dimethylamino)propyl]carbodiimide, N,N'-carbonyldiimidazole and N,N'-carbonyldithiazole.

15. A process according to claim 1, wherein said coupling agent is N,N'-dicyclohexylcarbodiimide.

16. A process according to claim 1, wherein said X is chloro.

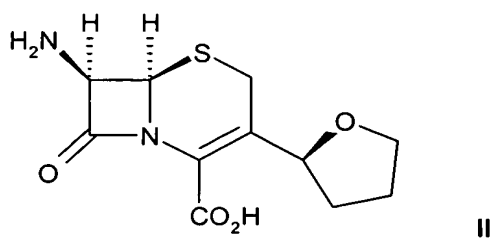
17. A process according to claim 2, wherein said R^3 is para-nitrobenzyl and said suitable deprotecting agent is sodium dithionite or a catalytic hydrogenating agent.

18. A process according to claim 2, wherein said R^3 is allyl and said suitable deprotecting agent is tetrakis triphenylphosphine palladium (0).

5 19. A process according to claim 17, wherein said solvent is acetone, water, tetrahydrofuran or mixtures thereof.

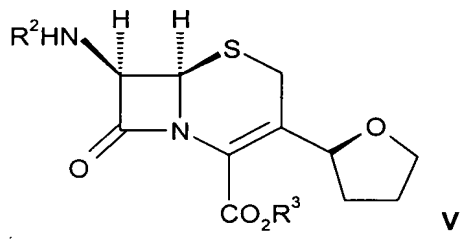
20. A process according to claim 4, wherein said solvent is methylene chloride, tetrahydrofuran or mixtures thereof.

21. A compound of formula II:



22. The compound according to claim 21 wherein said compound of the formula II has an enantiomeric or diastereomeric purity of 96% to 100%.

23. A compound of formula V:



15 wherein R^2 is acyl; and R^3 is para-nitrobenzyl or allyl.

24. The compound according to claim 23 wherein said compound of the formula V has an enantiomeric or diastereomeric purity of 96% to 100%.